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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 08/486,069 | 06/07/1995 | DEAN ENGELHARDT | ENZ-5(D8)(C2 | 6278 |
| 28171 | 7590 | 06/07/2005 | EXAMINER | |
| ENZO BIOCHEM, INC. 527 MADISON AVENUE (9TH FLOOR) NEW YORK, NY 10022 | | | MARSCHEL, ARDIN H | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1631 | |

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|--------------------------|--------------------------------------|--|--|
| Interview Summary | Application No. 08/486,069 | Applicant(s) ENGELHARDT ET AL. | |
| | Examiner Ardin Marschel | Art Unit 1631 | |
| | | | |

All participants (applicant, applicant's representative, PTO personnel):

(1) Ardin Marschel (Exr.)

(3) Gene Rzucidlo (Appl. Rep.)

(2) Ronald Fedus (Appl. Rep.)

(4) Rob Schulman (Appl. Rep.)

Date of Interview: 29 June 2005

(5) Michael Woodward (Gen.)

Type: a) ☐ Telephonic b) ☐ Video Conference
c) ☒ Personal [copy given to: 1) ☐ applicant

2) ☒ applicant's representative]

Exhibit shown or demonstration conducted: d) ☒ Yes e) ☒ No.

If Yes, brief description: See attached

Claim(s) discussed: all rejected

Identification of prior art discussed: N/A

Agreement with respect to the claims f) ☐ was reached. g) ☒ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See note below

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

We discussed possible claim amendments as attached to overcome the 112, 2nd para. reqn. with ~~cancelation~~ AM 6/29/05 of 1500-1503 to overcome the 112, 1st para. of these claims. We discussed the New Matter reqn regarding the different labels regarding sequencing.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Ardin Marschel

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Substance of the April 1, 2004 Interview

Engelhardt et al., Serial No. 08/486,069 (Filed June 7, 1995)

The April 1, 2004 interview was attended by Examiner Ardin H. Marschel, Group Art Unit 1631, Eugene C. Rzucidlo, Esq. of Greenberg Traurig (New York, NY), Dr. James J. Donegan, Applicants' representative and also a senior scientist for the assignee of Serial No. 08/486,069, and Ronald C. Fedus, Esq., Applicants' attorney of record. In the Interview Summary dated April 1, 2004, it is indicated that "[w]e discussed a number of possible claim amendments to overcome the rejections of record."

As described below, a number of matters were discussed at the April 1, 2004 interview.

Furanosyl

Applicants' representatives and attorney urged that in contrast to the term "furanose moiety," the term "furanosyl moiety" better describes the nature of the ring element in nucleic acid structure. The Examiner seemed willing to consider, if not accept, the proposed change in the claims from "furanose moiety" to "furanosyl moiety." Applicants' attorney indicated that in their next response the claims would be amended to reflect this change to "furanosyl moiety."

Nucleotide Analog

The matter of nucleotide analogs was also discussed at the April 1, 2004 interview. Applicants' attorney explained that the term "nucleotide analog" is a term long recognized in the art, as evidenced by the books authored by Prof. Dr. Karl Heinz Scheit [Nucleotide Analogs: Synthesis and Biological Function, John Wiley & Sons, New York, 1980], and Dr. Arthur Kornberg [DNA Synthesis, W. H. Freeman and Company, San Francisco, CA 1974; DNA Replication, also Freeman and Company,

1980; 1982 Supplement to DNA Replication, again, Freeman and Company].¹ Applicants' attorneys also pointed out that Kornberg's "nucleotide analogs" were defined as those molecules that could be incorporated into DNA or RNA. It was generally agreed at the April 1, 2004 interview that the term "nucleotide analog" could be recited in the claims, with additional embodiments or language directed to "base analogs," because Applicants' specification disclosed several examples of these. Applicants' attorney indicated that the claims would be amended in their next response to reflect the term "nucleotide analog," and that some dependent claims would be appropriately amended or presented to reflect the term "base analogs" and various related terms.

Indicator Molecule

The nature of "indicator molecule" had been raised in the July 1, 2003 Office Action (pages 8-9). It is believed that this matter was briefly discussed at the April 1, 2004 interview. It is also believed that Applicants' attorneys indicated that some amendments would be effected to the claims in order to clarify the relationship between the detectable non-radioactive moieties A or Sig and the indicator molecules.

Non-Nucleotidyl

At the April 1, 2004 interview, various pieces of prior art cited in the July 1, 2003 Office Action were discussed. Regarding the Dunn [Cell 12:23 (1977)] and Hartman [Biopolymers 20:2635 (1981)] documents, it was generally agreed that a description in the claims that the detectable non-radioactive moiety was *non-nucleotidyl* in nature, would probably overcome the prior art rejections. The Examiner did indicate, however, that a showing of support for the term "non-nucleotidyl" would be necessary. Applicants' attorneys indicated that the claims would be amended in their next response to reflect the "non-nucleotidyl" nature of

¹ These books are already of record in this application.

the detectable non-radioactive moiety. Applicants attorneys further indicated that a showing of support would be made in connection with those claim amendments.

With respect to claim 1411 in which the detection process is carried out with a non-radioactively detectable protein, it was generally agreed at the April 1, 2004 interview that the recitation of "operator sequence" in the claim would probably overcome the anticipation rejection by Kourilsky (P/N 4,581,333 and GB 2,019,408). At the April 1st interview, Applicants attorneys and representative indicated that "operator sequence" was being used in a classical sense, much as in Example XXXIV in the specification. The latter statement was made in response to the Examiner's query at the April 1, 2004 interview.

The interview then concluded.

* * * * *

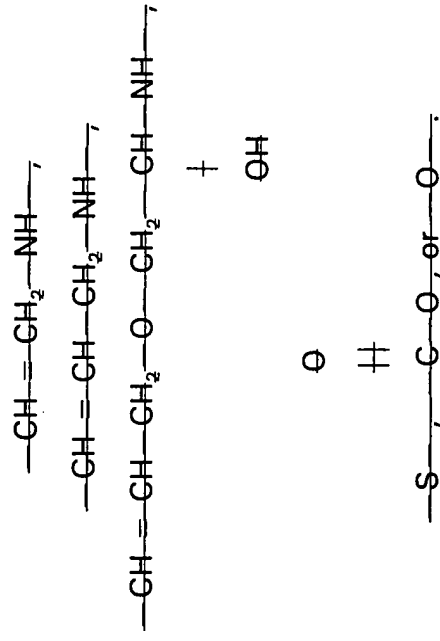
June 29, 2005

Proposed cancellation of claims 1500-1503 (with respect to the linkages for Sig attached to the phosphate & sugar)

Claim 1500 (TO BE CANCELED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a CH_2NH moiety, or both.

Claim 1501 (TO BE CANCELED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises an allylamine group.

Claim 1502 (TO BE CANCELED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



Enz-5(D8)(C2)

Claim 1503 (TO BE CANCELED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a glycosidic linkage moiety.

* * * * *

June 29, 2005

Enz-5(D8)(C2)

U.S. PAT. APPL. SER. NO. 08/486,069 (ENGELHARDT ET AL.)

Claims 1723-1724, 1740-1741, 1769-1773, 1775 & 1769

Directed to different or same indicator molecules

Claim 1723 (Pending) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with the same indicator molecules.

Claim 1724 (Pending) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with different indicator molecules.

Claim 1740 (Pending) The process of any of claims 657, 809, 961, 1113, or 1287, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are labeled with the same indicator molecules.

Claim 1741 (Pending) The process of any of claims 657, 809, 961, 1113, or 1287, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are labeled with different indicator molecules.

Claim 1769 (Pending) A process for determining the sequence of a nucleic acid of interest comprising:

- providing at least one nucleic acid of interest;
- generating detectable non-radioactively labeled nucleic acid fragments complementary to said nucleic acid of interest or a portion thereof, wherein said fragments have been labeled by incorporation of one or more nucleoside triphosphates comprising different fluorescent indicators;
- subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and
- detecting said separated or resolved fragments by means of said different fluorescent-indicators, to determine the sequence of said nucleic acid of interest.

Claim 1770 (Pending) The process according to claim 1769, wherein in said generating step, said modified or labeled nucleoside triphosphates comprise a furanosyl moiety.

Claim 1771 (Pending) The process according to claim 1770, wherein said furanosyl moiety comprises a ribose, 2'-deoxyribose, 3'-deoxyribose or 2',3'-dideoxyribose.

Claim 1772 (Pending) The process according to claim 1769, wherein in said generating step, said different fluorescent indicators comprise fluorescein, rhodamine or dansyl.

Claim 1773 (Pending) The process according to claim 1769, wherein in said generating step, said one or more nucleoside triphosphates comprise a base moiety or a base analog comprising a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, a pyrimidine, or a pyrimidine analog.

Claim 1775 (Pending) The process according to claim 1773, wherein the fluorescent or chemiluminescent indicators in said modified or labeled nucleoside triphosphates are attached to said purine, said purine analog, said 7-deazapurine, said 7-deazapurine analog, said pyrimidine, or said pyrimidine analog.

Claim 1796 (Pending) A process for determining the sequence of a nucleic acid of interest comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising: (a) a sequence complementary to said nucleic acid of interest or a portion thereof, and (b) different fluorescent labels covalently attached, directly or through a linkage group, to said fragments;

subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments;

detecting non-radioactively said separated or resolved fragments by means of said attached different fluorescent labels; and

determining the sequence of said nucleic acid of interest from said detected fragments.

* * * * *

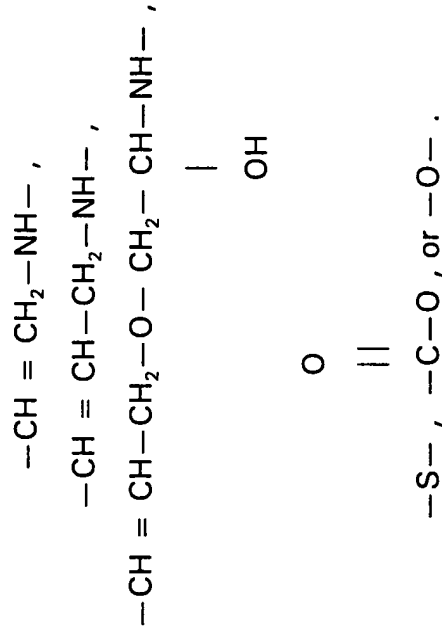
Proposed amendments to claims 1436-1439 & 1441-1444

Rejected for Vagueness/Indefiniteness (Lack of Antecedent Basis)

Claim 1436 (PROPOSED AMENDMENT) The process according to claim 1432, wherein, ~~in said nucleotide structure or nucleotide analog structure (i)~~, said covalent attachment comprises an olefinic bond at the α -position relative to the point of attachment to said nucleotide structure or nucleotide analog structure (i) , a $\text{CH}_2\text{NH}-$ moiety, or both.

Claim 1437 (PROPOSED AMENDMENT) The process according to claim 1436, wherein, ~~in said nucleotide structure or nucleotide analog structure (i)~~, said covalent attachment comprises an allylamine group.

Claim 1438 (PROPOSED AMENDMENT) The process according to claim 1436, wherein, ~~in said nucleotide structure or nucleotide analog structure (i)~~, said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



Claim 1439 (PROPOSED AMENDMENT) The process according to claim 1432, wherein, ~~in said nucleotide structure or nucleotide analog structure (i),~~ said covalent attachment comprises a glycosidic linkage moiety.

Claim 1441 (PROPOSED AMENDMENT) The process according to claim 1440, wherein, ~~in said nucleotide structure or nucleotide analog structure (i),~~ said covalent attachment is through a linkage group.

Claim 1442 (PROPOSED AMENDMENT) The process according to claim 1441, wherein, ~~in said nucleotide or nucleotide analog structure (i),~~ said linkage group comprises an amine.

Claim 1443 (PREVIOUSLY PRESENTED -- REMAINS UNAMENDED) The process according to claim 1442, wherein said amine comprises a primary amine.

Claim 1444 (PREVIOUSLY PRESENTED -- REMAINS UNAMENDED) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said operator sequence.

* * * * *